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* * * * * * * * * *  Welcome to STN International  * * * * * * * * * *

 NEWS  1          Web Page URLs for STN Seminar Schedule - N. America
 NEWS  2  Apr 08  "Ask CAS" for self-help around the clock
 NEWS  3  Apr 09  BEILSTEIN: Reload and Implementation of a New Subject Area
 NEWS  4  Apr 09  ZDB will be removed from STN
 NEWS  5  Apr 19  US Patent Applications available in IFICDB, IFIPAT, and IFIUDB
 NEWS  6  Apr 22  Records from IP.com available in CAPLUS, HCAPLUS, and ZCAPLUS
 NEWS  7  Apr 22  BIOSIS Gene Names now available in TOXCENTER
 NEWS  8  Apr 22  Federal Research in Progress (FEDRIP) now available
 NEWS  9  Jun 03  New e-mail delivery for search results now available
 NEWS 10  Jun 10  MEDLINE Reload
 NEWS 11  Jun 10  PCTFULL has been reloaded
 NEWS 12  Jul 02  FOREGE no longer contains STANDARDS file segment
 NEWS 13  Jul 22  USAN to be reloaded July 28, 2002;
                  saved answer sets no longer valid
 NEWS 14  Jul 29  Enhanced polymer searching in REGISTRY
 NEWS 15  Jul 30  NETFIRST to be removed from STN
 NEWS 16  Aug 08  CANCERLIT reload
 NEWS 17  Aug 08  PHARMAMarketLetter(PHARMAML) - new on STN
 NEWS 18  Aug 08  NTIS has been reloaded and enhanced
 NEWS 19  Aug 19  Aquatic Toxicity Information Retrieval (AQUIRE)
                  now available on STN
 NEWS 20  Aug 19  IFIPAT, IFICDB, and IFIUDB have been reloaded
 NEWS 21  Aug 19  The MEDLINE file segment of TOXCENTER has been reloaded
 NEWS 22  Aug 26  Sequence searching in REGISTRY enhanced
 NEWS 23  Sep 03  JAPIO has been reloaded and enhanced
 NEWS 24  Sep 16  Experimental properties added to the REGISTRY file
 NEWS 25  Sep 16  Indexing added to some pre-1967 records in CA/CAPLUS
 NEWS 26  Sep 16  CA Section Thesaurus available in CAPLUS and CA
 NEWS 27  Oct 01  CASREACT Enriched with Reactions from 1907 to 1985

 NEWS EXPRESS  February 1 CURRENT WINDOWS VERSION IS V6.0d,
               CURRENT MACINTOSH VERSION IS V6.0a(ENG) AND V6.0Ja(JP),
               AND CURRENT DISCOVER FILE IS DATED 05 FEBRUARY 2002
 NEWS HOURS    STN Operating Hours Plus Help Desk Availability
 NEWS INTER    General Internet Information
 NEWS LOGIN    Welcome Banner and News Items
 NEWS PHONE    Direct Dial and Telecommunication Network Access to STN
 NEWS WWW      CAS World Wide Web Site (general information)

Enter NEWS followed by the item number or name to see news on that
specific topic.

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  * * * * * * * * * * * * * * STN  Columbus  * * * * * * * * * * * * * * *


FILE 'HOME' ENTERED AT 09:26:48 ON 11 OCT 2002

=> file reg
COST IN U.S. DOLLARS                            SINCE FILE      TOTAL
                                                   ENTRY    SESSION
FULL ESTIMATED COST                                 0.21       0.21
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FILE 'REGISTRY' ENTERED AT 09:26:58 ON 11 OCT 2002
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PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
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Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES:    9 OCT 2002  HIGHEST RN 460312-12-3
DICTIONARY FILE UPDATES:   9 OCT 2002  HIGHEST RN 460312-12-3

TSCA INFORMATION NOW CURRENT THROUGH MAY 20, 2002

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

Crossover limits have been increased.  See HELP CROSSOVER for details.

Experimental and calculated property data are now available.  See HELP
PROPERTIES for more information.  See STNote 27, Searching Properties
in the CAS Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

=> e pramipexole/cn
E1            1     PRAMINDOLE/CN
E2            1     PRAMINO/CN
E3            1 --> PRAMIPEXOLE/CN
E4            1     PRAMIPEXOLE DIHYDROCHLORIDE/CN
E5            1     PRAMIPEXOLE DIHYDROCHLORIDE MONOHYDRATE/CN
E6            1     PRAMIRACETAM/CN
E7            1     PRAMIRACETAM HYDROCHLORIDE/CN
E8            1     PRAMIRACETAM SULFATE/CN
E9            1     PRAMITOL/CN
E10           1     PRAMITOL 5P/CN
E11           1     PRAMIVERINE/CN
E12           1     PRAMLINTIDE/CN

=> s e3
L1            1 PRAMIPEXOLE/CN

=> d l1

L1   ANSWER 1 OF 1  REGISTRY  COPYRIGHT 2002 ACS
RN   104632-26-0  REGISTRY
CN   2,6-Benzothiazolediamine, 4,5,6,7-tetrahydro-N6-propyl-, (6S)- (9CI)  (CA
     INDEX NAME)
OTHER CA INDEX NAMES:
CN   2,6-Benzothiazolediamine, 4,5,6,7-tetrahydro-N6-propyl-, (S)-
OTHER NAMES:
CN   (-)-Pramipexole
CN   Pramipexole
CN   SND 919
CN   SUD-919CL2Y
CN   U 98528E
FS   STEREOSEARCH
MF   C10 H17 N3 S
CI   COM
SR   CA
LC   STN Files:   ADISINSIGHT, ADISNEWS, BEILSTEIN*, BIOBUSINESS, BIOSIS,
       BIOTECHNO, CA, CANCERLIT, CAPLUS, CBNB, CIN, DDFU, DIOGENES, DRUGNL,
       DRUGPAT, DRUGU, DRUGUPDATES, EMBASE, IPA, MEDLINE, MRCK*, PHAR, PROMT,
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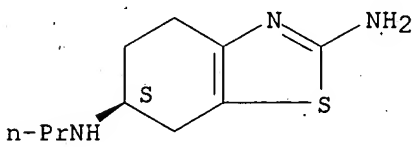
SYNTHLINE, TOXCENTER, USAN, USPAT2, USPATFULL
(*File contains numerically searchable property data)
Other Sources: WHO

Absolute stereochemistry. Rotation (-).



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

179 REFERENCES IN FILE CA (1962 TO DATE)
1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
179 REFERENCES IN FILE CAPLUS (1962 TO DATE)

```
=> e lamotrigine/cn
E1            1     LAMOTANE-X/CN
E2            1     LAMOTRIGIN/CN
E3            1 --> LAMOTRIGINE/CN
E4            1     LAMOTRIGINE HYDRATE/CN
E5            1     LAMOTRIGINE ISETHIONATE/CN
E6            1     LAMOTRIGINE MESYLATE/CN
E7            1     LAMOTRIGINE N2-GLUCURONIDE/CN
E8            1     LAMOUROUXIDE I/CN
E9            1     LAMOXACTAM/CN
E10           1     LAMOXIRENE/CN
E11           1     LAMOXY/CN
E12           1     LAMP BLACK 101/CN

=> s e3
L2            1 LAMOTRIGINE/CN

=> s l2
L3            1 LAMOTRIGINE/CN

=> e diazepam/cn
E1            1     DIAZENYLOXYGEN(1+)/CN
E2            1     DIAZEP/CN
E3            1 --> DIAZEPAM/CN
E4            1     DIAZEPAM 3-HYDROXYLASE/CN
E5            1     DIAZEPAM BINDING INHIBITOR (HUMAN)/CN
E6            1     DIAZEPAM BINDING INHIBITOR-(39-75)/CN
E7            1     DIAZEPAM BINDING INHIBITOR-RELATED PROTEIN (HUMAN CLONE DRS-
                    1)/CN
E8            1     DIAZEPAM BINDING-INHIBITING PROTEINS/CN
E9            1     DIAZEPAM C3 HYDROXYLASE/CN
E10           1     DIAZEPAM DIPICRYLAMINATE/CN
E11           1     DIAZEPAM HEXABROMOTELLURATE/CN
E12           1     DIAZEPAM HYDROCHLORIDE/CN

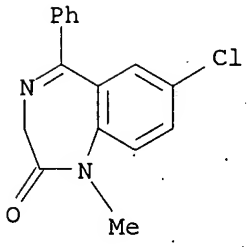
=> s e3
L4            1 DIAZEPAM/CN

=> d l4

L4   ANSWER 1 OF 1  REGISTRY  COPYRIGHT 2002 ACS
```

RN 439-14-5 REGISTRY
CN 2H-1,4-Benzodiazepin-2-one, 7-chloro-1,3-dihydro-1-methyl-5-phenyl- (8CI, 9CI) (CA INDEX NAME)
OTHER NAMES:
CN 1-Methyl-5-phenyl-7-chloro-1,3-dihydro-1H-1,4-benzodiazepin-2-one
CN 1-Methyl-5-phenyl-7-chloro-1,3-dihydro-2H-1,4-benzodiazepin-2-one
CN 7-Chloro-1,3-dihydro-1-methyl-5-phenyl-2H-1,4-benzodiazepin-2-one
CN 7-Chloro-1-methyl-2-oxo-5-phenyl-3H-1,4-benzodiazepine
CN 7-Chloro-1-methyl-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one
CN 7-Chloro-1-methyl-5-phenyl-3H-1,4-benzodiazepin-2(1H)-one
CN An-Ding
CN Ansiolisina
CN Apaurin
CN Apozepam
CN Assival
CN Atensine
CN Atilen
CN Bialzepam
CN Calmocitene
CN Calmpose
CN Cercine
CN Ceregulart
CN Diacepan
CN Diapam
CN Diazemuls
CN **Diazepam**
CN Diazepam-Lipuro
CN Duxen
CN Eridan
CN Faustan
CN Horizon
CN LA 111
CN Lembrol
CN Levium
CN Methyldiazepinone
CN Methyldiazepinone (pharmaceutical)
CN Morosan
CN Noan
CN Org 2447
CN Paxate
CN Paxel
CN Quievita
CN Relaminal
CN Relanium
CN Ro 5-2807
CN Saromet
CN Seduxen
CN Setonil
CN Sibazon
CN Sibazone
CN Sonacon
CN Stesolid
CN Stesolin
CN Tranimul
ADDITIONAL NAMES NOT AVAILABLE IN THIS FORMAT - Use FCN, FIDE, or ALL for DISPLAY
FS 3D CONCORD
DR 11100-37-1, 53320-84-6
MF C16 H13 Cl N2 O
CI COM
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, AQUIRE, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CABA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CBNB,

CEN, CHEMCATS, CHEMINFORMRX, CHEMLIST, CIN, CSCHEM, CSNB, DDFU, DETHERM*, DIOGENES, DRUGPAT, DRUGU, EMBASE, GMELIN*, HODOC*, HSDB*, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, MSDS-OHS, NIOSHTIC, PHAR, PHARMASEARCH, PIRA, PROMT, RTECS*, SPECINFO, TOXCENTER, TULSA, ULIDAT, USAN, USPAT2, USPATFULL, VETU
(*File contains numerically searchable property data)
Other Sources: DSL**, EINECS**, TSCA**, WHO
(**Enter CHEMLIST File for up-to-date regulatory information)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

11389 REFERENCES IN FILE CA (1962 TO DATE)
58 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
11396 REFERENCES IN FILE CAPLUS (1962 TO DATE)
55 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

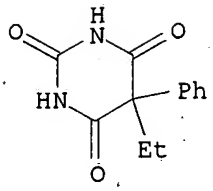
```
=> e phenobarbital/cn
E1            1     PHENOBAL SODIUM/CN
E2            1     PHENOBAR/CN
E3            1 --> PHENOBARBITAL/CN
E4            1     PHENOBARBITAL 2-THIOSEMICARBAZONE/CN
E5            2     PHENOBARBITAL CALCIUM/CN
E6            1     PHENOBARBITAL COMPOUND WITH ISOPROPYLANTIPYRINE/CN
E7            1     PHENOBARBITAL COMPOUND WITH PICOLINAMIDE (2:3)/CN
E8            1     PHENOBARBITAL DIETHYLAMINE SALT/CN
E9            1     PHENOBARBITAL MAGNESIUM/CN
E10           1     PHENOBARBITAL MONOHYDRATE/CN
E11           1     PHENOBARBITAL QUINIDINE/CN
E12           1     PHENOBARBITAL SILVER SALT/CN

=> s e3
L5            1 PHENOBARBITAL/CN

=> d l5

L5   ANSWER 1 OF 1  REGISTRY  COPYRIGHT 2002 ACS
RN   50-06-6  REGISTRY
CN   2,4,6(1H,3H,5H)-Pyrimidinetrione, 5-ethyl-5-phenyl- (9CI)  (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN   Barbituric acid, 5-ethyl-5-phenyl- (8CI)
OTHER NAMES:
CN   5-Ethyl-5-phenylbarbituric acid
CN   5-Phenyl-5-ethylbarbituric acid
CN   Adonal
CN   Agrypnal
CN   Amylofene
CN   Barbenyl
CN   Barbiphenyl
CN   Barbipil
```

CN Barbita
CN Barbivis
CN Blu-phen
CN Cratecil
CN Dormiral
CN Doscalun
CN Duneryl
CN Eskabarb
CN Etilfen
CN Euneryl
CN Fenemal
CN Gardenal
CN Gardepanyl
CN Hysteps
CN Lepinal
CN Lepinaletten
CN Liquital
CN Lixophen
CN Lubergal
CN Luminal
CN Neurobarb
CN Noptil
CN Nunol
CN Phenaemal
CN Phenemal
CN Phenobar
CN **Phenobarbital**
CN Phenobarbitone
CN Phenobarbituric acid
CN Phenoluric
CN Phenonyl
CN Phenylethylbarbituric acid
CN Phenylethylmalonylurea
CN Phenyral
CN Phob
CN Sedonal
CN Sedophen
CN Sevenal
CN Somonal
CN Stental Extentabs
CN Teolaxin
ADDITIONAL NAMES NOT AVAILABLE IN THIS FORMAT - Use FCN, FIDE, or ALL for DISPLAY
FS 3D CONCORD
DR 11097-06-6, 46755-67-3
MF C12 H12 N2 O3
CI COM
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, AQUIRE, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CABA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CHEMINFORMRX, CHEMLIST, CIN, CSCHEM, CSNB, DDFU, DETHERM*, DIOGENES, DRUGU, EMBASE, GMELIN*, HODOC*, HSDB*, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, MSDS-OHS, NIOSHTIC, PHARMASEARCH, PIRA, PROMT, RTECS*, SPECINFO, SYNTHLINE, TOXCENTER, USAN, USPAT2, USPATFULL, VETU
(*File contains numerically searchable property data)
Other Sources: DSL**, EINECS**, WHO
(**Enter CHEMLIST File for up-to-date regulatory information)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

12942 REFERENCES IN FILE CA (1962 TO DATE)
80 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
12948 REFERENCES IN FILE CAPLUS (1962 TO DATE)
95 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

```
=> e valproic acid/cn
E1            1     VALPROATE SEMISODIUM/CN
E2            1     VALPROATE SODIUM/CN
E3            1 --> VALPROIC ACID/CN
E4            1     VALPROIC ACID ANHYDRIDE/CN
E5            1     VALPROIC ACID CALCIUM SALT/CN
E6            1     VALPROIC ACID CHLORIDE/CN
E7            1     VALPROIC ACID ETHYL ESTER/CN
E8            1     VALPROIC ACID GLUCURONIDE/CN
E9            1     VALPROMIDE/CN
E10           1     VALPROYL CHLORIDE/CN
E11           1     VALPROYL-COA OXIDASE/CN
E12           1     VALPROYLCARNITINE/CN

=> s e3
L6            1 "VALPROIC ACID"/CN

=> d l6

L6   ANSWER 1 OF 1  REGISTRY  COPYRIGHT 2002 ACS
RN   99-66-1  REGISTRY
CN   Pentanoic acid, 2-propyl- (9CI)  (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN   Valeric acid, 2-propyl- (6CI, 7CI, 8CI)
OTHER NAMES:
CN   2-Propylpentanoic acid
CN   2-Propylvaleric acid
CN   4-Heptanecarboxylic acid
CN   Acetic acid, dipropyl-
CN   Depakine
CN   Dipropylacetic acid
CN   DPA
CN   Ergenyl
CN   n-Dipropylacetic acid
CN   Valproic acid
FS   3D CONCORD
MF   C8 H16 O2
CI   COM
LC   STN Files:   ADISNEWS, AGRICOLA, ANABSTR, AQUIRE, BEILSTEIN*, BIOBUSINESS,
       BIOSIS, BIOTECHNO, CA, CABA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CBNB,
       CHEMCATS, CHEMLIST, CHEMSAFE, CIN, CSCHEM, CSNB, DDFU, DETHERM*,
       DIOGENES, DRUGU, EMBASE, HSDB*, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE,
       MRCK*, NIOSHTIC, PHAR, PHARMASEARCH, PROMT, RTECS*, SPECINFO, SYNTHLINE,
       TOXCENTER, USAN, USPAT2, USPATFULL
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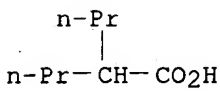
(*File contains numerically searchable property data)
Other Sources: EINECS**, WHO
(**Enter CHEMLIST File for up-to-date regulatory information)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

3131 REFERENCES IN FILE CA (1962 TO DATE)
114 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
3133 REFERENCES IN FILE CAPLUS (1962 TO DATE)
7 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

=> file caplus

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	32.60	32.81

FILE 'CAPLUS' ENTERED AT 09:30:28 ON 11 OCT 2002
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
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FILE COVERS 1907 - 11 Oct 2002 VOL 137 ISS 16
FILE LAST UPDATED: 10 Oct 2002 (20021010/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

CAS roles have been modified effective December 16, 2001. Please check your SDI profiles to see if they need to be revised. For information on CAS roles, enter HELP ROLES at an arrow prompt or use the CAS Roles thesaurus (/RL field) in this file.

=> d his

(FILE 'HOME' ENTERED AT 09:26:48 ON 11 OCT 2002)

FILE 'REGISTRY' ENTERED AT 09:26:58 ON 11 OCT 2002
E PRAMIPEXOLE/CN
L1 1 S E3
E LAMOTRIGINE/CN
L2 1 S E3

```
L3              1 S L2
                E DIAZEPAM/CN
L4              1 S E3
                E PHENOBARBITAL/CN
L5              1 S E3
                E VALPROIC ACID/CN
L6              1 S E3

     FILE 'CAPLUS' ENTERED AT 09:30:28 ON 11 OCT 2002

=> s l1
L7            179 L1

=> s l2
L8            576 L2

=> s l3 or l4 or l5 or l6
              576 L3
            11418 L4
            13055 L5
             3134 L6
L9          26061 L3 OR L4 OR L5 OR L6

=> s l7 and l9
L10             9 L7 AND L9

=> s l7 and anticonvulsant##
            18484 ANTICONVULSANT##
L11             0 L7 AND ANTICONVULSANT##

=> s l7 and cocaine
            16515 COCAINE
L12             8 L7 AND COCAINE

=> s cocaine and l9
            16515 COCAINE
L13           405 COCAINE AND L9

=> s l13 and l7
L14             0 L13 AND L7

=> s l3 and withdrawl
           687950 l3
              123 WITHDRAWL
L15             3 l3 AND WITHDRAWL

=> d l10 1-9 bib,ab

L10  ANSWER 1 OF 9  CAPLUS  COPYRIGHT 2002 ACS
AN   2002:555334  CAPLUS
DN   137:114525
TI   Syntactic deformable pharmaceutical foam compositions
IN   Odidi, Isa; Odidi, Amina
PA   Can.
SO   PCT Int. Appl., 47 pp.
     CODEN: PIXXD2
DT   Patent
LA   English
FAN.CNT 1
     PATENT NO.         KIND  DATE          APPLICATION NO.  DATE
     ---------------    ----  --------      ---------------  --------
PI   WO 2002056861      A2    20020725      WO 2002-CA54     20020117
```

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI US 2001-765783 A 20010119

AB The invention relates to methods for prepg. a syntactic foam compn. suitable for use as a carrier for chems. or other compds., including pharmaceuticals. Carbopol 971P, hydroxyethyl cellulose, cellulose microspheres and silica, was mixed in a high-shear mixer. The resulting admixt. was treated with 2-propanol, while simultaneously subjecting the admixt. to high-shear forces in the high-shear mixer. This mixing created a uniform stable syntactic deformable and compressible dendritic solid foam which could be shaped before drying. Metoprolol succinate was added to the above admixt. and subjected to high-shear agitation for 2 min before treatment with 2-propanol. A stable syntactic deformable and compressible dendritic solid foam which could be shaped before drying was obtained. This was dried at 40.degree.. The dried foam was the disentangled by size redn. to obtain discrete particles. The free flowing particles were reassembled and shaped by compression in a mold. The shaped units, when subjected to an aq. medium, released metoprolol over a period of .ltoreq.3 h.

L10 ANSWER 2 OF 9 CAPLUS COPYRIGHT 2002 ACS

AN 2002:354556 CAPLUS

DN 137:98838

TI Molecular Properties That Influence the Oral Bioavailability of Drug Candidates

AU Veber, Daniel F.; Johnson, Stephen R.; Cheng, Hung-Yuan; Smith, Brian R.; Ward, Keith W.; Kopple, Kenneth D.

CS Departments of Medicinal Chemistry, Cheminformatics, Computational Analytical and Structural Sciences, and Drug Metabolism and Pharmacokinetics, GlaxoSmithKline, King of Prussia, PA, 19406-0939, USA

SO Journal of Medicinal Chemistry (2002), 45(12), 2615-2623
CODEN: JMCMAR; ISSN: 0022-2623

PB American Chemical Society

DT Journal

LA English

AB Oral bioavailability measurements in rats for over 1100 drug candidates studied at Smith-Kline Beecham Pharmaceuticals (now Glaxo Smith-Kline) have allowed us to analyze the relative importance of mol. properties considered to influence that drug property. Reduced mol. flexibility, as measured by the no. of rotatable bonds, and low polar surface area or total hydrogen bond count (sum of donors and acceptors) are found to be important predictors of good oral bioavailability, independent of mol. wt. That on av. both the no. of rotatable bonds and polar surface area or hydrogen bond count tend to increase with mol. wt. may in part explain the success of the mol. wt. parameter in predicting oral bioavailability. The commonly applied mol. wt. cutoff at 500 does not itself significantly sep. compds. with poor oral bioavailability from those with acceptable values in this extensive data set. Our observations suggest that compds. which meet only the 2 criteria of (1) 10 or fewer rotatable bonds and (2) polar surface area .ltoreq.140 ANG 2 (or 12 or fewer H-bond donors and acceptors) will have a high probability of good oral bioavailability in the rat. Data sets for the artificial membrane permeation rate and for clearance in the rat were also examd. Reduced polar surface area correlates better with increased permeation rate than does lipophilicity

(C log P), and increased rotatable bond count has a neg. effect on the permeation rate. A threshold permeation rate is a prerequisite of oral bioavailability. The rotatable bond count does not correlate with the data examd. here for the in vivo clearance rate in the rat.

RE.CNT 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 3 OF 9 CAPLUS COPYRIGHT 2002 ACS
AN 2002:276810 CAPLUS
DN 136:395832
TI Influence of benzodiazepines on antiparkinsonian drug treatment in levodopa users
AU van de Vijver, D. A. M. C.; Roos, R. A. C.; Jansen, P. A. F.; Porsius, A. J.; de Boer, A.
CS Department of Pharmacoepidemiology and Pharmacotherapy, Utrecht Institute for Pharmaceutical Sciences (UIPS), Utrecht University, Utrecht, 3508 TB, Neth.
SO Acta Neurologica Scandinavica (2002), 105(1), 8-12
CODEN: ANRSAS; ISSN: 0001-6314
PB Blackwell Munksgaard
DT Journal
LA English
AB Animal studies showed that benzodiazepines decrease the concn. of dopamine in the striatum. Benzodiazepines may therefore affect the treatment of Parkinson's disease. This study detd. whether start of a benzodiazepine in patients on levodopa was followed by a faster increase of antiparkinsonian drug treatment. Data came from the PHARMO database, which includes information on drug dispensing for all residents of six Dutch cities. Selected were all patients aged 55 yr and older who used levodopa for at least 360 days. The rate of increase of antiparkinsonian drug treatment was compared between starters of a benzodiazepine and controls who did not start a benzodiazepine with the use of Cox's proportional hazard model. Identified were 45 benzodiazepine starters (27 women, mean age 76.4 yr) and 169 controls (83 women, 74.3 yr). Antiparkinsonian drug treatment increased faster in the benzodiazepine group; relative risk was 1.44 (95% confidence interval 0.80-2.59). This study has not found any statistically significant increase in antiparkinsonian drug treatment when a benzodiazepine was started in a small population of chronic levodopa users.

RE.CNT 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 4 OF 9 CAPLUS COPYRIGHT 2002 ACS
AN 2002:276280 CAPLUS
DN 136:304024
TI Method for determining chemical reactivity
IN Wienkers, Larry C.; Hauer, Michael J.; Epps, Dennis E.
PA Pharmacia & Upjohn Company, USA
SO PCT Int. Appl., 25 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2002029416	A2	20020411	WO 2001-US27754	20011005

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

	AU 2001096234	A5	20020415	AU 2001-96234	20011005
	US 2002110919	A1	20020815	US 2001-972520	20011005
PRAI	US 2000-238238P	P	20001005		
	WO 2001-US27754	W	20011005		

AB A process for screening chem. compds. for electrophilic properties comprising the steps of: (a) providing an assay having one or more reaction vessels; (b) adding a predetd. amt. of sep. chem. compds. for screening to each reaction vessel; (c) adding a predetd. amt. of a surrogate chem. marker to each reaction vessel and allowing said sep. chem. compds. and surrogate chem. marker to incubate for a period of time; (d) adding a reactive chem. to each reaction vessel which is capable of reacting with residual surrogate chem. marker such that the amt. of residual surrogate chem. marker present after step (c) can be quant. or qual. measured; and (e) quant. or qual. measuring said residual chem. marker is provided. In particular, the invention provides a high throughput toxicity screening method for pharmaceutically active mols.

L10 ANSWER 5 OF 9 CAPLUS COPYRIGHT 2002 ACS
AN 2001:622393 CAPLUS
DN 135:339134
TI Adjunctive dopamine agonists in treatment-resistant Bipolar-II-depression: an open case series
AU Perugi, G.; Toni, C.; Ruffolo, G.; Frare, F.; Akiskal, H.
CS Department of Psychiatry, University of Pisa, Pisa, Italy
SO Pharmacopsychiatry (2001), 34(4), 137-141
CODEN: PHRMEZ; ISSN: 0176-3679
PB Georg Thieme Verlag
DT Journal
LA English
AB Objective: Previous studies and case observations have suggested that dopamine agonists (DAAs) such as pramipexole (PPX) and ropinirole (RPN) might be effective for major depression, but their adjunctive use in treatment-resistant bipolar-II-depression has not yet been specifically addressed. Method: A chart review was conducted on 18 patients with a DSM-III-R bipolar NOS (Bipolar II) major depressive episode who were admitted to the day-hospital of the Department of Psychiatry at the University of Pisa. DAAs were added to ongoing treatments with conventional antidepressants and mood stabilizers to which patients had no responded after a period of at least 8 wk. Clin. state and adverse effects were assessed at each visit. Final improvement in CGI scores of 1 or 2 were considered as responders. Results: Mean DAA trial duration was 17.6 (sd = 7.8, range 4-34) weeks, with a mean final dose of 1.23.+-.0.32 mg/day (range, 0.75-1.50 mg/day) for PPX, and 2.97.+-.0.99 mg/day (range, 1.50-5.00 mg/day) for RPN. DAAs were well tolerated and did not show any neg. interaction with concomitant psychotropic medications. Only one patient became worse (final CGI = 5), and had to interrupt PPX due to nausea, increased agitation and irritability. Eight patients (44.4%) were considered responders (4 with PPX and 4 with RPN): 5 showed marked improvement (CGI = 1), and 3 showed moderate improvement (CGI = 2); another 5 (27.8%) manifested a transient response not sustained up to the end. The initial and final scores of CGI severity scale for all patients (responders and non-responders combined) were, resp., 5.33.+-.0.7 and 3.94.+-.1.3 (mean .+-. S.D). The mean change according to the CGI severity scale was statistically significant ($t = 4.74$, $p < 0.0002$). Conclusion: From the results, PPX and RPN appear to be well tolerated and potentially useful in the adjunctive treatment of drug-resistant bipolar II depression.
RE.CNT 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 6 OF 9 CAPLUS COPYRIGHT 2002 ACS
AN 2001:338762 CAPLUS
DN 134:362292
TI Methods of determining individual hypersensitivity to a pharmaceutical agent from gene expression profile
IN Farr, Spencer
PA Phase-1 Molecular Toxicology, USA
SO PCT Int. Appl., 222 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2001032928	A2	20010510	WO 2000-US30474	20001103
WO 2001032928	A3	20020725		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRAI US 1999-165398P P 19991105
US 2000-196571P P 20000411

AB The invention discloses methods, gene databases, gene arrays, protein arrays, and devices that may be used to det. the hypersensitivity of individuals to a given agent, such as drug or other chem., in order to prevent toxic side effects. In one embodiment, methods of identifying hypersensitivity in a subject by obtaining a gene expression profile of multiple genes assocd. with hypersensitivity of the subject suspected to be hypersensitive, and identifying in the gene expression profile of the subject a pattern of gene expression of the genes assocd. with hypersensitivity are disclosed. The gene expression profile of the subject may be compared with the gene expression profile of a normal individual and a hypersensitive individual. The gene expression profile of the subject that is obtained may comprise a profile of levels of mRNA or cDNA. The gene expression profile may be obtained by using an array of nucleic acid probes for the plurality of genes assocd. with hypersensitivity. The expression of the genes predetd. to be assocd. with hypersensitivity is directly related to prevention or repair of toxic damage at the tissue, organ or system level. Gene databases arrays and app. useful for identifying hypersensitivity in a subject are also disclosed.

L10 ANSWER 7 OF 9 CAPLUS COPYRIGHT 2002 ACS
AN 2000:725436 CAPLUS
DN 133:301171
TI Compositions and methods for improved delivery of ionizable hydrophobic therapeutic agents
IN Chen, Feng-jing; Patel, Manesh V.
PA Lipocine, Inc., USA
SO PCT Int. Appl., 99 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

PI WO 2000059475 A1 20001012 WO 2000-US7342 20000316
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
US 6383471 B1 20020507 US 1999-287043 19990406
EP 1165048 A1 20020102 EP 2000-916547 20000316
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO
PRAI US 1999-287043 A 19990406
WO 2000-US7342 W 20000316

AB The present invention is directed to a pharmaceutical compn. including a hydrophobic therapeutic agent having at least one ionizable functional group, and a carrier. The carrier includes an ionizing agent capable of ionizing the functional group, a surfactant, and optionally solubilizers, triglycerides, and neutralizing agents. The invention further relates to a method of prepg. such compns. by providing a compn. of an ionizable hydrophobic therapeutic agent, an ionizing agent, and a surfactant, and neutralizing a portion of the ionizing agent with a neutralizing agent. The compns. of the invention are particularly suitable for use in oral dosage forms. A carrier contg. concd. phosphoric acid 0.025, Tween-20 0.3, Arlacel 186 0.2, sodium taurocholate 0.15, propylene glycol 0.3 g was formulated. Itraconazole was included in the carrier at 30 mg/mL for testing the stability of the itraconazole soln. upon diln. in simulated gastric fluid.

RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 8 OF 9 CAPLUS COPYRIGHT 2002 ACS
AN 2000:720729 CAPLUS
DN 136:256719
TI QSAR model for drug human oral bioavailability. [Erratum to document cited in CA133:159633]
AU Yoshida, Fumitaka; Topliss, John G.
CS Division of Medicinal Chemistry College of Pharmacy, University of Michigan, Ann Arbor, MI, 48109-1065, USA
SO Journal of Medicinal Chemistry (2000), 43(24), 4723
CODEN: JMCMAR; ISSN: 0022-2623
PB American Chemical Society
DT Journal
LA English

AB On page 2578, Table 5, the correct footnote e is as follows: "e Weighting is 0.5, where the carbon .alpha. to the carbonyl is tertiary, or the carbonyl is attached to a ring with ortho substituents on each side, or the carbonyl can undergo intramol. hydrogen bonding with a nearby group.". On page 2580, in Table 6, under the "structural descriptors" column, the correct data for entries 96 and 133 is 7, 13 for both compds. Under the "drug" column, the correct spelling of the names for entries 83 and 107 are propranolol and chlorthalidone, resp.

L10 ANSWER 9 OF 9 CAPLUS COPYRIGHT 2002 ACS
AN 2000:375684 CAPLUS
DN 133:159633
TI QSAR Model for Drug Human Oral Bioavailability
AU Yoshida, Fumitaka; Topliss, John G.
CS Division of Medicinal Chemistry College of Pharmacy, University of Michigan, Ann Arbor, MI, 48109-1065, USA

SO Journal of Medicinal Chemistry (2000), 43(13), 2575-2585
CODEN: JMCMAR; ISSN: 0022-2623
PB American Chemical Society
DT Journal
LA English
AB The quant. structure-bioavailability relationship of 232 structurally diverse drugs was studied to evaluate the feasibility of constructing a predictive model for the human oral bioavailability of prospective new medicinal agents. The oral bioavailability detd. in human adults was assigned one of four ratings and analyzed in relation to physicochem. and structural factors by the ORMUCS (ordered multicategorical classification method using the simplex technique) method. A systematic examn. of various physicochem. parameters relating primarily to absorption, and structural elements which could influence metab., was carried out to analyze their effects on the bioavailability classification of drugs in the data set. Lipophilicity, expressed as the distribution coeff. at pH 6.5, was found to be a significant factor influencing bioavailability. The observation that acids generally had better bioavailability characteristics than bases, with neutral compds. between, led to the formulation of a new parameter, .DELTA. log D (log D6.5 - log D7.4), which proved to be an important contributor in improving the classification results. The addn. of 15 structural descriptors relating primarily to well-known metabolic processes yielded a satisfactory QSAR equation which had a correct classification rate of 71% (97% within one class) and a Spearman rank correlation coeff. (Rs) of 0.851, despite the diversity of structure and pharmacol. activity in the compd. set. In leave-one-out tests, an av. of 67% of drugs were correctly classified (96% within one class) with an Rs of 0.812. The relationship formulated identified significant factors influencing bioavailability and assigned them quant. values expressing their contribution. The predictive power of the model was evaluated using a sep. test set of 40 compds., of which 60% (95% within one class) were correctly classified. Since the necessary physicochem. parameters can be calcd. or estd. and the structural descriptors are obtained from an inspection of the structure, the model enables a rough est. to be made of the prospective human oral bioavailability of unsynthesized compds. Also, the model has the advantage of transparency in that it indicates which factors may affect bioavailability and the extent of that effect. This could be useful in designing compds. which are more bioavailable. Refinement of the model is possible as more bioavailability data becomes available. Potential uses are in drug design, prioritization of compds. for synthesis, and selection for detailed studies of early compd. leads in drug discovery programs.
RE.CNT 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d his

(FILE 'HOME' ENTERED AT 09:26:48 ON 11 OCT 2002)

FILE 'REGISTRY' ENTERED AT 09:26:58 ON 11 OCT 2002
E PRAMIPEXOLE/CN
L1 1 S E3
E LAMOTRIGINE/CN
L2 1 S E3
L3 1 S L2
E DIAZEPAM/CN
L4 1 S E3
E PHENOBARBITAL/CN
L5 1 S E3
E VALPROIC ACID/CN
L6 1 S E3

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     FILE 'CAPLUS' ENTERED AT 09:30:28 ON 11 OCT 2002
L7           179 S L1
L8           576 S L2
L9         26061 S L3 OR L4 OR L5 OR L6
L10            9 S L7 AND L9
L11            0 S L7 AND ANTICONVULSANT##
L12            8 S L7 AND COCAINE
L13          405 S COCAINE AND L9
L14            0 S L13 AND L7
L15            3 S 13 AND WITHDRAWL

=> d l12 1-8 bib,ab

L12  ANSWER 1 OF 8  CAPLUS  COPYRIGHT 2002 ACS
AN   2001:498645  CAPLUS
DN   135:282531
TI   Clinical efficacy of pramipexole in the treatment of conditions other than
     Parkinson's disease
AU   Becker, Philip M.; Corrigan, Mark H.; Kasper, Siegfried; Lin, Siong-Chi;
     Montplaisir, Jacques; Szegedi, A.; Willner, Paul
CS   One Glen Lakes, Dallas, TX, 75231, USA
SO   Reviews in Contemporary Pharmacotherapy (2001), 12(1 & 2), 87-104
     CODEN: RCPHFW; ISSN: 0954-8602
PB   Marius Press
DT   Journal; General Review
LA   English
AB   A review, with refs.  The non-ergot dopamine receptor agonist,
     pramipexole, which shows affinity for the D2 and D3 subtypes of the D2
     dopamine receptor subfamily, with preference for the D3 receptor, is
     currently licensed for the treatment of advanced-stage Parkinson's disease
     in the European Union, and for both early and advanced-stage Parkinson's
     disease in the USA and Canada.  There are, however, intriguing reports
     that this agent may also have other beneficial clin. effects on symptoms
     assocd. with, or occurring independently of, Parkinson's disease.  It has
     been shown that depression, which is a frequent accompaniment of
     Parkinson's disease, may not necessarily be simply an emotional reaction
     to the parkinsonian symptoms but could be etiopathol. linked to the same
     underlying dopaminergic mechanisms.  There is evidence that pramipexole
     can alleviate mild-to-moderate depression, whether or not this occurs in
     assocn. with Parkinson's disease.  Such findings may throw interesting new
     light on the involvement of dopaminergic processes in depressive illness.
     Pramipexole may also have an antianxiety potential, though currently it is
     not clear whether this is secondary to, or independent of, its
     antidepressive actions.  Although some studies have been conducted on
     possible antischizophrenic effects of pramipexole, these have generally
     been small and have either given neg. results or have suggested that the
     treatment may alleviate neg. schizophrenic symptoms, with effects on pos.
     symptoms being less evident.  Pramipexole is a potent treatment for
     restless-legs syndrome (RLS), a dose of 0.375-0.75 mg/day producing
     complete relief of symptoms in the majority of cases.  Other conditions in
     which pramipexole might be expected to produce some clin. improvements
     include attention-deficit-hyperactivity disorder, sexual impotence in
     males, cocaine addiction, and supranuclear palsy, though no
     direct evidence currently exists to support any of these putative
     applications.  Exploration of the profile of clin. effectiveness of
     pramipexole may be expected to throw interesting new light on the
     interrelationships between a range of neurol. and neuropsychiatric
     conditions.
RE.CNT  163   THERE ARE 163 CITED REFERENCES AVAILABLE FOR THIS RECORD
              ALL CITATIONS AVAILABLE IN THE RE FORMAT
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L12 ANSWER 2 OF 8 CAPLUS COPYRIGHT 2002 ACS
AN 2001:498642 CAPLUS
DN 135:282529
TI Mechanisms of action of pramipexole: Effects on receptors
AU Dziedzicka-Wasylewska, Marta; Ferrari, Francesca; Johnson, Reuben D.; Mierau, Joachim; Rogoz, Zofia; Skuza, Grazyna; Sokoloff, Pierre
CS Institute of Pharmacology, Polish Academy of Sciences, Krakow, 31-343, Pol.
SO Reviews in Contemporary Pharmacotherapy (2001), 12(1 & 2), 1-31
CODEN: RCPHFW; ISSN: 0954-8602
PB Marius Press
DT Journal; General Review
LA English
AB A review with refs. Pramipexole, a tetrahydrobenzothiazole compd., has selective affinity for dopamine receptors of the D2 subfamily, with a 7-10-fold greater affinity for D3 than for D2 receptor subtypes; affinity for the D4 receptor subtype is 17-fold less than for D3 receptors. The available exptl. evidence suggests that, in intact normofunctional dopaminergic systems, pramipexole exerts its primary effects on presynaptic dopamine autoreceptors, probably of both D2 and D3 subtypes, as a result of which it suppresses the synthesis and synaptic release of dopamine; effects on postsynaptic receptors are elicited only at higher dose levels and with substantially longer latencies than are needed for presynaptic autoreceptor stimulation. However, in dopaminergic systems in which dopamine release is reduced, as a result of presynaptic neuron degeneration or destruction, or by other means, postsynaptic dopamine D2 and D3 receptors are much more readily stimulated by pramipexole. These receptor effects of pramipexole may be linked to its established or putative therapeutic effects in conditions related to reduced levels of dopamine release. Thus, it is proposed that, in Parkinson's disease, pramipexole readjusts the balance between direct and indirect striatopallidal outflow pathways which, acting together, modulate the inhibition/facilitation of motor activity; this occurs as a result of the stimulation of both D2 and D3 postsynaptic receptors in dopamine depleted circuits. Pramipexole has been reported to have beneficial effects against depression, an action which seems likely to reflect pramipexole-induced stimulation of postsynaptic dopamine D2 receptors; this same effect in frontal cortical regions may reduce the neg. symptoms of schizophrenia. Pramipexole may also exert therapeutic effects in certain states of dopaminergic dysfunction which do not involve reduced levels of dopamine. The suppression of dopamine release in mesolimbic regions, resulting from the stimulation by pramipexole of presynaptic dopamine D2 autoreceptors, may lead to pos. therapeutic effects in schizophrenia and anxiety disorders. Pramipexole may find some clin. role as an adjunct to treatment programs aimed at reducing **cocaine** abuse. Further elucidation of the effects which pramipexole is able to elicit at the level of dopamine receptors in different brain regions will not only provide valuable insights into the role of dopaminergic mechanisms in a range of neuropsychiatric dysfunctions, but will lead to the further refinement of effective therapies for such conditions.
RE.CNT 318 THERE ARE 318 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 3 OF 8 CAPLUS COPYRIGHT 2002 ACS
AN 2001:293416 CAPLUS
DN 135:102451
TI Antagonism of the discriminative stimulus effects of (+)-7-OH-DPAT by remoxipride but not PNU-99194A
AU Christian, A. J.; Goodwin, A. K.; Baker, L. E.
CS Department of Psychology, Western Michigan University, Kalamazoo, MI, 49008, USA
SO Pharmacology, Biochemistry and Behavior (2001), 68(3), 371-377

CODEN: PBBHAU; ISSN: 0091-3057
PB Elsevier Science Inc.
DT Journal
LA English
AB The dopamine (DA) agonist 7-hydroxy-N,N-di-n-propyl-2-amino-tetralin (7-OH-DPAT) has been used extensively as a tool to investigate the role of DA D3 receptors in the reinforcing and discriminative stimulus properties of psychostimulant drugs. The present study examd. the relative importance of D3 vs. D2 receptor actions in the discriminative stimulus effects of (+)-7-OH-DPAT (0.03 mg/kg, s.c.) in 16 male Sprague-Dawley rats trained to discriminate this compd. from saline in a two-lever, water-reinforced operant procedure under a FR 20 schedule. Stimulus generalization and antagonism tests were conducted with **cocaine** and with various selective D2 and D3 receptor ligands. In contrast to previous findings that (+)-7-OH-DPAT substitutes for **cocaine**, the present results demonstrated that **cocaine** does not produce stimulus generalization in animals trained to discriminate (+)-7-OH-DPAT. Although two D3-preferring agonists, PD-128907 and pramipexole, produced complete stimulus generalization to the training drug, two highly selective D3 antagonists (PNU-99194A, PD 152255) failed to block the discriminative stimulus effects of (+)-7-OH-DPAT. However, the D2 antagonist remoxipride (3.0 mg/kg) produced a rightward shift in the (+)-7-OH-DPAT dose-response curve. These findings suggest that D2 receptors are critically involved in mediating the cue properties of (+)-7-OH-DPAT. However, alternative interpretations that PNU-99194A is not entirely D3 receptor selective should also be considered.
RE.CNT 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 4 OF 8 CAPLUS COPYRIGHT 2002 ACS
AN 2001:247120 CAPLUS
DN 134:247272
TI Use of pramipexole as a treatment for **cocaine** craving
IN Rosenbaum, Jerrold
PA The General Hospital Corporation, USA
SO PCT Int. Appl., 15 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2001022820	A1	20010405	WO 2000-US26634	20000928

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRAI US 1999-156860P P 19990930
AB Disclosed are methods for reducing stimulant dependency or craving, involving administration of a dopamine agonist, such as pramipexole.
RE.CNT 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 5 OF 8 CAPLUS COPYRIGHT 2002 ACS
AN 1997:521361 CAPLUS
DN 127:171508
TI D3-receptor test in vitro predicts decreased **cocaine**

self-administration in rats
AU Caine, S. Barak; Koob, George F.; Parsons, Loren H.; Everitt, Barry J.; Schwartz, Jean-Charles; Sokoloff, Pierre
CS Department of Neuropharmacology, The Scripps Research Institute, La Jolla, CA, USA
SO NeuroReport (1997), 8(9-10), 2373-2377
CODEN: NERPEZ; ISSN: 0959-4965
PB Rapid Science Publishers
DT Journal
LA English
AB The three dopamine agonists with highest reported D3 receptor selectivity in vitro, pramipexole, quinelorane and PD128,907, decreased self-administration of a high dose of **cocaine** in rats as a result of a leftward shift in the **cocaine** dose-effect function. In contrast the D3 preferring antagonist nafadotride increased **cocaine** self-administration. Moreover the relative potencies of these and other D2-like dopamine agonists (lisuride, 7-OH-DPAT, quinpirole, apomorphine, bromocriptine) to modulate **cocaine** self-administration were highly correlated with their relative potencies for increasing mitogenesis in vitro in cell lines expressing D3 but not D2 receptors. These results support the hypothesis that the D3 receptor may be an important target for pharmacotherapies for **cocaine** abuse and dependence.

L12 ANSWER 6 OF 8 CAPLUS COPYRIGHT 2002 ACS
AN 1997:255615 CAPLUS
DN 126:312164
TI Involvement of dopamine receptors in the antipsychotic profile of (-)-eticlopride
AU Giuliani, Daniela; Ferrari, Francesca
CS Department of Biomedical Sciences, Section of Pharmacology, University of Modena, Modena, 41100, Italy
SO Physiology & Behavior (1997), 61(4), 563-567
CODEN: PHBHA4; ISSN: 0031-9384
PB Elsevier
DT Journal
LA English
AB The present study was performed to assess the effects exerted by the dopamine (DA) D2/D3 antagonist (-) eticlopride on rodent behavioral models considered to be predictive of antipsychotic activity, namely, antagonism toward DA agonist-induced stereotyped behavior (SB), and ketamine- and **cocaine**-induced hypermotility. (-) Eticlopride (10-50 .mu.g/kg) dose-dependently inhibited SB elicited by SND 919 (10 mg/kg), CQP 201-403 (0.5 mg/kg), and 7-OH-DPAT (5 mg/kg); moreover, it significantly counteracted the hypermotility induced in rats and mice by ketamine (5 and 10 mg/kg). When (-) eticlopride was injected before **cocaine** (15 mg/kg) either acutely or subchronically administered in male rats, it also potently antagonized the hypermotility typically induced by the drug. These results are discussed in the light of putative D2/D3 receptor involvement, and are considered as predictive of antipsychotic potential.

L12 ANSWER 7 OF 8 CAPLUS COPYRIGHT 2002 ACS
AN 1996:144658 CAPLUS
DN 124:250639
TI Influence of eticlopride on **cocaine**- and DA D2 agonist-induced behavioral effects in rats
AU Ferrari, F.; Giuliani, D.
CS Dep. Biomed. Sci., Univ. Modena, Modena, 41100, Italy
SO Pharmacology, Biochemistry and Behavior (1996), 53(3), 525-30
CODEN: PBBHAU; ISSN: 0091-3057
PB Elsevier
DT Journal

LA English
AB The influence of the DA D2 antagonist (-)-eticlopride on **cocaine** - and DA D2 agonist-induced behavioral effects was investigated by means of two series of expts., in rats. In the first 10-day series, coadministration of (-)-eticlopride (10 and 50 .mu.g/kg, SC) always potently inhibited **cocaine** (15 mg/kg, IP)-induced hypermotility but did not modify the penile erection (PE)-enhancement produced by the drug at the first injection; it actually counteracted the inhibitory effect of subchronic **cocaine** on PE. In the second series, (-)-eticlopride, at the same doses, antagonized PE elicited by various DA D2 agonists at nonstereotyping doses; when, along with PE, stereotyped behavior was induced, only the latter was inhibited by (-)-eticlopride, which even increased PE.

L12 ANSWER 8 OF 8 CAPLUS COPYRIGHT 2002 ACS
AN 1991:598533 CAPLUS
DN 115:198533
TI Use of dopamine autoreceptor agonists in the treatment of drug dependency
IN Kutter, Eberhard; Schingnitz, Guenter
PA Boehringer Ingelheim K.-G., Germany; Boehringer Ingelheim International G.m.b.H.
SO Eur. Pat. Appl., 13 pp.
CODEN: EPXXDW
DT Patent
LA German
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 417637	A2	19910320	EP 1990-117147	19900906
	EP 417637	A3	19920902		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
	DE 3930282	A1	19910321	DE 1989-3930282	19890911
	DD 297557	A5	19920116	DD 1990-343855	19900906
	CA 2025003	AA	19910312	CA 1990-2025003	19900910
	JP 03106825	A2	19910507	JP 1990-239790	19900910
	HU 57584	A2	19911230	HU 1990-5853	19900910
PRAI	DE 1989-3930282		19890911		

AB BHT 920 (I) and SND 919 (II) and their acid addn. salts are dopamine autoreceptor agonists (i.e. decrease the synthesis and release of dopamine from cells of the mesolimbic and nigrostriatal system) and thus are useful in treatment of drug-dependence mediated by dopamine release. By diminishing the pos. reinforcement of drug consumption resulting from dopamine release in these brain centers and the consequent euphoric inner reward, I and II prevent craving for the drug. The action of I and II is enhanced by their activity on supersensitive postsynaptic D2-dopaminergic receptors in dopamin-depleted chronic drug abusers, as well as by their central .alpha.2-adrenergic activity. I and II themselves do not induce dependence. Thus, in monkeys allowed to self-administer **cocaine**, the self-administration rate decreased to 0 after i.v. injection of I (0.1 mg/kg, twice). Pills were prepd. contg. I 50 .mu.g, lactose 38.45, corn starch 10.0, gelatin 1.0, and Mg stearate 0.5 mg.

=> d his

(FILE 'HOME' ENTERED AT 09:26:48 ON 11 OCT 2002)

FILE 'REGISTRY' ENTERED AT 09:26:58 ON 11 OCT 2002
E PRAMIPEXOLE/CN
L1 1 S E3
E LAMOTRIGINE/CN
L2 1 S E3

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L3              1 S L2
                  E DIAZEPAM/CN
L4              1 S E3
                  E PHENOBARBITAL/CN
L5              1 S E3
                  E VALPROIC ACID/CN
L6              1 S E3

     FILE 'CAPLUS' ENTERED AT 09:30:28 ON 11 OCT 2002
L7            179 S L1
L8            576 S L2
L9          26061 S L3 OR L4 OR L5 OR L6
L10             9 S L7 AND L9
L11             0 S L7 AND ANTICONVULSANT##
L12             8 S L7 AND COCAINE
L13           405 S COCAINE AND L9
L14             0 S L13 AND L7
L15             3 S 13 AND WITHDRAWL

=> d l15 1-3 bib,ab

L15  ANSWER 1 OF 3  CAPLUS  COPYRIGHT 2002 ACS
AN   1979:533922  CAPLUS
DN   91:133922
TI   Beta-blocker withdrawal syndrome
AU   Botting, J. H.; Gibson, A.
CS   Dep. Pharmacol., Chelsea Coll., London, Engl.
SO   Lancet (1979), 1(8121), 875-6
     CODEN: LANCAO; ISSN: 0023-7507
DT   Journal
LA   English
AB   Rats, given propranolol  [525-66-6] (40-50 mg/kg/day in drinking water for
     12-13 days), followed by 2 days on normal tap water, were
     .apprx.4 times as sensitive to isoprenaline  [7683-59-2] as controls,
     probably because of the prodn. of denervation supersensitivity.  Since
     denervation supersensitivity decays with reinervation, treatment with
     long-acting .beta.-blockers may be of value, causing the return of normal
     sensitivity more or less in parallel with a slowly decaying
     .beta.-adrenoceptor blockade.

L15  ANSWER 2 OF 3  CAPLUS  COPYRIGHT 2002 ACS
AN   1976:29972  CAPLUS
DN   84:29972
TI   Isolated CH stretching frequencies, bond properties, and Fermi resonances
     in some methyl-nitrogen single bond compounds
AU   McKean, D. C.; Ellis, I. A.
CS   Dep. Chem., Univ. Aberdeen, Aberdeen, Scot.
SO   J. Mol. Struct. (1975), 29(1), 81-96
     CODEN: JMOSB4
DT   Journal
LA   English
AB   CHD2-substituted derivs. are prepd. and their IR spectra recorded for the
     following compds.: MeNH2, Me2NH, Me3N, Me2NSiH3, Me2NSiF3 and (Me2N)2SiF2.
     The isolated CH stretching frequency for the CH bond trans to the N
     unshared pair varies markedly with the substitution and can be correlated
     with the first ionization potential.  It offers a useful indication of the
     extent of electron withdrawl by Si; the CH stretching spectrum
     for (CHD2)2NSiF3 is consistent with a planar C2NSi skeleton.  Calcns. for
     the CH3, CD3 and CHD2 species in the amines enable a quant. description to
     be given of the Bohlmann bands near 2800 cm-1.  These are fundamentals,
     displaced by Fermi resonances to the extent of .apprx. 30, 20, and 10
     cm-1, resp., for MeNH2, Me2NH and (CD3)2NMe, which are primarily motions
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involving stretching of the weak CH bond. D0298 Values predicted for the two CH bonds in each Me group of Me3N differ by .apprx. **13** kcal mole-1.

L15 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2002 ACS
AN 1974:10351 CAPLUS
DN 80:10351
TI Azidomorphine and rymazolium [Probon]. Approach to the ideal analgesic
AU Knoll, J.
CS Dep. Pharmacol., Semmelweis Med. Univ., Budapest, Hung.
SO Pharmacol. Res. Commun. (1973), 5(2), 175-91
CODEN: PLRCAT
DT Journal
LA English
AB Azidomorphine (I) [22952-87-0] was .sim.300 times more potent and azidocodeine [22958-08-3] was .sim.**13** times more potent than morphine [57-27-2] in the hot plate test in rats. I administered to rats over a 10-week period was less toxic than morphine. In the jumping test severe withdrawl symptoms could be elicited in mice receiving 40 times the analgesic ED50 dose of morphine, whereas only moderate dependence occurred in mice receiving 2800 times the analgesic ED50 dose of I. Increasing morphine doses induced high levels of tolerance and phys. dependence in rats and monkeys. Severe abstinence symptoms were elicited by nalorphine treatment on the 24th day and by abrupt **withdrawl** of morphine on the 55th, 176th, and 300th days of treatment. No tolerance or phys. dependence occurred in rats and monkeys during parallel expts. with increasing equianalgesic doses of I. MZ 144 (rymazolium) [28610-84-6], a non-narcotic analgesic strongly potentiated the analgesic effects of both I and azidocodeine. Use of the combination analgesic may provide clin. relief from severe acute or chronic pain without the risks of addiction and tolerance inherent in morphine analgesia.